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86. Menthatrienes and the Oxidation of Limonene

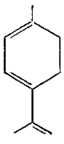
By **Alan F. Thomas** and **Waltraud Bucher**

Research Laboratories, *Firmenich & Cie.*, 1211 Genève 8

(1. IV. 70)

Summary. The oxidation of limonene with mercuric acetate gives a mixture containing mentha-1.3.8-triene, the hydrocarbon of parsley, and its isomer, mentha-1.4.8-triene. Selenium dioxide oxidation of limonene in alcohol gives as the main product mentha-1.8-dien-4-ol, and pyrolysis of the acetate of the latter, or of mentha-1.8-dien-10-yl acetate (the main product of the oxidation of limonene with selenium dioxide in acetic anhydride), also gives a mixture of menthatrienes. A discussion of the selenium dioxide oxidation of limonene is presented.

Mentha-1,3,8-triene (**1**) has been isolated from parsley (*Petroselinum sativum Hoffm.*), and reported to have the typical odour of the plant [1]. Another menthatriene (the 1.5.8-isomer) has been prepared on at least three occasions [2] [3] [4], but the properties of the three preparations were never compared, and in one case [3] not even recorded. A synthesis of mentha-1.3.8-triene (**1**) and of its isomer, mentha-1.4.8-triene (**2**), has been described by *Birch & Subba Rao*, but they apparently did not obtain their products in a pure state, and spectral characterization of mentha-1.4.8-triene was confined to an ultraviolet spectrum [5]. Recently, it was reported that mentha-1,8-dien-10-yl acetate (**3**) occurs in the peel oil of *Citrus unishu*, and is formed by the action of selenium dioxide in acetic anhydride on limonene [6]. Since this compound is involved in the preparation of the menthatrienes described below, and because the Japanese work [6] on the synthesis was confined to a footnote, we are presenting here our own work on the preparation of this substance.[1]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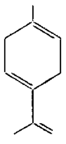
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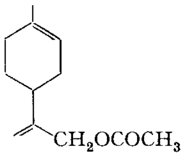
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The early reports [7] about the reaction of limonene with selenium dioxide were not substantiated by spectral data, and we have undertaken a fresh study of the

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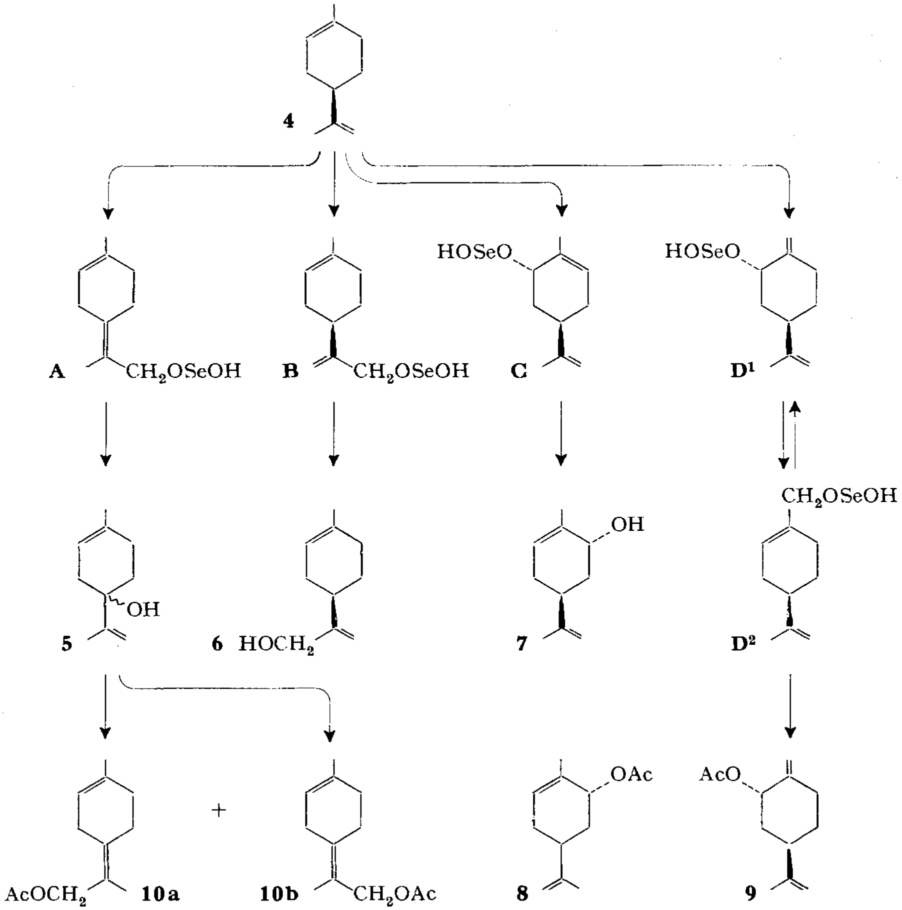
[1] *Added in proof:* Some of the results described here and notably the isolation of **5**, have been recently reported by *Sakuda* [6a].

reaction. In ethanol, (+)-limonene (**4**) reacts with selenium dioxide to give racemic mentha-1.8-dien-4-ol (**5**) as the main product, together with some (+)-mentha-1.8-dien-10-ol (**6**), and optically active carveol (**7**). The latter was shown to be a mixture of about 5:1 *trans:cis* by acetylation of the carveol fraction and gas-liquid chromatography of the acetates. The *trans*-acetate prepared in this way had a rotation of + 144°, corresponding to about 80% retention of configuration, based on the rotation of *trans*-carveyl acetate quoted by *Johnston & Read* [8]. In analogy to the results of *Büchi & Wüest* on the reaction of selenium dioxide with optically active carvone [9], the tertiary alcohol **5** is the expected product, and, also like the carvone product, is a racemate.

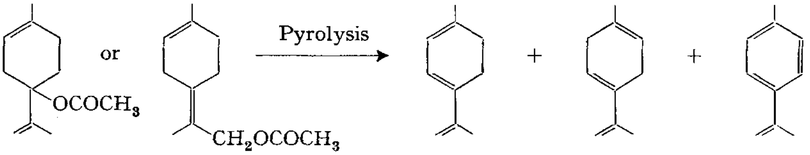


These facts can be readily accounted for in the light of the results obtained by *Wiberg & Nielsen* on the selenium dioxide oxidation of (+)-menth-1-ene, when they obtained a carvotanacetone with 44–55% retention of stereochemistry [10], using the detailed mechanism discussed by *Schaefer et al.* [11]. The attack of selenium dioxide on a double bond in a cyclohexane system occurs so that oxygen is initially inserted into the axial position, and the axial allylic proton is abstracted (leading in the case of (+)-limonene to the selenium(II) ester **C**). Bimolecular displacement by the water present in the mixture now occurs through an S_N2' path, leading to mainly the axial *trans*-carveol (**7**). *Schaefer et al.* used this reasoning [11] to explain the partial retention of configuration observed in the selenium oxide oxidation of (+)-menth-3-ene [12], which *Ohloff* & *Uhde* found to be about 76% racemized in the course of the oxidation [13] – a loss of chirality that is much higher than we found with limonene. Formation of the major product (**5**) must proceed through the intermediate **A**, on which the displacement can occur from either side of the molecule, resulting in the racemate **5**. In order to give mentha-1.8-dien-10-ol (**6**), the initially formed selenium(II) ester **B** is itself of the same chirality as the original (+)-limonene, and the S_N2' displacement does not involve the chiral centre (C-4) so that the product is optically active. This product **6** is, incidentally, the same as the compound obtained by pyrolysis of the product of the reaction of (+)-limonene (**4**) with lead tetraacetate [14].

The selenium dioxide oxidation of (+)-limonene in acetic anhydride takes a different course; not more than a trace of the tertiary alcohol **5** is formed, the principal products being carveyl acetates (**8**) in nearly the same ratio of *trans:cis* (4:1) as when ethanol is used as solvent, but now almost optically inactive, mentha-1.8-dien-10-yl acetate (**3**), and *trans*-mentha-1(7),8-dien-2-yl acetate (**9**).

It was noticed by *Wiberg* & *Nielsen* that selenium dioxide oxidation in acetic acid gave racemic products, but optically active ones in alcohol [10], and the mechanism discussed by *Schaefer et al.* [11] requires allylic rearrangements of the intermediate selenium esters (e.g. **C**) to occur in solvents like acetic acid, where ion-pair formation occurs. The formation of *trans*-mentha-1(7),8-dien-2-yl acetate (**9**) also requires the intervention of an allylic rearrangement, since the initially formed selenium ester $\mathbf{D}^1$ would give rise to an aldehyde after an S_N2' displacement. The allylically rearrangement ester $\mathbf{D}^2$, however, will lead to the observed product by S_N2' displacement, and it will be expected that this compound will be optically active. We found a rotation of + 71°, in fact, which is somewhat higher than that reported by *Naves* & *Grampoloff* [2] for the acetate of what they believed to be the *cis*-isomer of **9**, but which was shown later to be actually the *trans*-isomer [15].

Treatment of the alcohol **5** with phosphorus tribromide in the presence of pyridine, followed by hydrolysis with potassium acetate in acetone2) [16], gave a mixture of the $\Delta^{4(8)}$-9- and $\Delta^{4(8)}$-10-acetates (**10a** and **10b**), recognisable as a mixture by the double signal in the NMR. spectrum for the methylene group carrying the acetyl function. Finally the acetate **11** of the tertiary alcohol **5** was made by acetylation of the alcohol with a mixture of acetyl chloride and acetic anhydride in dimethylaniline.



11 **10a+10b** **1** **2** **12**

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2) We are greatly indebted to Dr. *K.-H. Schulte-Elte* and Mr. *M. Pawlak* for a sample of the acetates **10** prepared in this way.

Pyrolysis of either acetate **11**, or the mixture of acetates **10**, led to a mixture that was separated by preparative gas chromatography into the three hydrocarbons to which structures **1**, **2** and **12** were attributed. Two different stationary phases are necessary for this separation because isopropenyltoluene (**12**) has the same retention time as the 1.3.8-triene (**1**) on non-polar (silicone oil) columns, and the same retention time as the 1.4.8-triene (**2**) on polar (Carbowax) columns. The proportions of the three hydrocarbons from the pyrolyses are about equal in both cases.

We have also found that oxidation of limonene with mercuric acetate [17] (conveniently carried out by direct distillation of the two together) also yields a small amount of hydrocarbon mixture, from which the 1.4.8-triene (**2**) can be isolated, but in which only small amounts of the 1.3.8-triene (**1**) were observed.

The structural attribution of the trienes **1** and **2** was deduced from their spectra. As might be expected, their mass spectra were very similar (though not identical), and correspond with the formula $C_{10}H_{14}$. The triene with the shorter retention time on both columns had a NMR. spectrum that was practically identical with that described by the French authors for the natural product [1]. The NMR. spectrum of the other triene was completely different, although still having the same functional groups. There were two methyl groups attached to double bonds, and four hydrogens on carbon atoms situated between two double bonds, and whose chemical shift of 2.71 ppm is close to that of the corresponding hydrogens in γ-terpinene (2.61 ppm). In addition, there were two vinyl hydrogens and two methylene hydrogens on a double bond. The UV. spectrum of this triene had a maximum at 236.5 nm ($\varepsilon_{max} =$ 11950), characteristic of a conjugated diene, but the conjugated triene **1** has its ultraviolet maximum at 303 nm ($\varepsilon_{max} = 14173$), in agreement with the structure proposed, and with the figures given by *Birch & Subba Rao* [5].

Only the fully conjugated triene possesses a distinct odour, but it is reminiscent of parsley only at high dilution. When concentrated, its odour is more naphthalenic, or even cresolic.

Experimental Section

Infrared spectra were taken with a *Perkin-Elmer* type 125 spectrophotometer. Ultraviolet spectra were measured with an *Optica* type CF4 NI instrument. Nuclear magnetic resonance spectra were measured in CCl_4 solution with tetramethylsilane as internal standard on a *Varian* A-60 spectrometer. Mass spectra were obtained with the *Atlas* CH4 instrument, using an inlet temperature of about 150° and electrons of 70 eV energy. Gas chromatography was carried out on a *Carlo Erba* type GT gas chromatograph, or (for preparative work) on a *Carlo Erba* "Fractovap" type P. Distillations were generally done using the *Nester-Faust* "Auto-annular" Teflon spinning band column.

Reaction of (+)*-limonene with selenium dioxide.* – *a*) To 274 g of (+)-limonene warmed to 50° was added dropwise a hot solution of 110 g of selenium dioxide dissolved in 180 ml of ethanol. After the addition (30 min), the mixture was stirred for a further 2 hr at 95–96°, then allowed to cool. The precipitated selenium (16 g) was removed by filtration, then washed with ethanol and ether, and the combined organic solutions concentrated. A rapid distillation separated 69 g of low boiling material (mostly unchanged limonene) from 38 g of a fraction with bp. 52–64°/0.1 Torr) that consisted mainly of (±)*-4-hydroxymentha-1.8-diene* (**5**). This fraction was carefully redistilled on the spinning band column, when 25 g of pure **5** were obtained, bp. 50°/0,01 Torr); n_D^{20} 1.4967; d_4^{20} 0.9527; α_D 0°. NMR. spectrum (ppm): 1.65 (m, $J < 2$ Hz, 3H, $C\mathit{H}_3\text{–}\overset{\diagup}{\mathrm{C}}\text{=}$), 1.75 ($s$, 3H, $C\mathit{H}_3\text{–}\overset{\diagup}{\mathrm{C}}\text{=}$), 4.72 ($m$, $J < 2$ Hz, 1H) and 4.90 (s, 1H, $>\mathrm{C}{=}\mathrm{C}\mathit{H}_2$), 5.22 (broad, 1H, $-\mathrm{CH}_2\text{–}\mathrm{C}\mathit{H}{=}\mathrm{C}<$). Mass spectrum, *m/e* (%): 69 (100), 84 (86), 41 (55), 43 (30), 39 (25); fragments at *m/e* 53, 55, 67, 68, 77, 79, 83, 91, 93, 94, 97, 109, 119, 123, 124, 137 (10–20), 152 ($M^{+\cdot}$, 13).

$C_{10}H_{16}O$ Calc. C 78.89 H 10.59% Found C 78.59 H 10.52%

The residue of this distillation was separated into two crude fractions, later shown to be crude *trans* + *cis*-carveol (6 g) and (+)-mentha-1.8-dien-10-ol (12 g), bp. 65° /0.01Torr, α_D^{20} + 112° (neat), identical in all respects with authentic material. In addition, the mp. of the *3.5-dinitrobenzoate* was undepressed when mixed with material obtained from the lead tetraacetate oxidation of (+)-limonene but not reported: mp. 72–72.5° (hexane).

$C_{17}H_{18}N_2O_6$ Calc. C 58.95 H 5.24 N 8.09% Found C 59.07 H 5.54 N 8.18%

The carveol fraction was acetylated with acetic anhydride in pyridine, and the mixture of acetates was shown by analytical gas chromatography to consist of *trans*- and *cis*-carveyl acetates in the ratio of 5:1. After redistillation on the spinning band column, a sample of (+)-*trans*-carveyl acetate was obtained that still contained a few % of the *cis*-isomer, α_D^{20} + 144° (neat).

b) A mixture of 13.6 g of (+)-limonene and 50 ml of acetic anhydride was heated to 80°, then 11.2 g of selenium dioxide were added in small portions. The temperature rose slowly to 104°, then was allowed to fall to 80°, and was maintained for a further hour at 80–90°. The precipitated selenium was filtered, and the filtrate was poured into 250 g of ice mixed with 25 ml of alcohol. After shaking for a few minutes, the mixture was extracted with pentane, and the pentane extracts washed with water, then a saturated solution of sodium hydrogen carbonate, then with water. Concentration and distillation gave 7.5 g of a mixture with bp. 51–75°/0.01 Torr. Gas chromatographic analysis showed that this mixture was very complex, but the three main components were isolated and characterized spectrally. They were carveyl acetate (40%, *trans* : *cis*), the *trans*-component of which had α_D^{20} + 6.8°, mentha-1.8-dien-10-yl acetate (30%), and *trans*-mentha-1(7).8-dien-2-yl acetate (20%). The latter had the following characteristics: $[\alpha]_D^{23}$ + 71° (chl). NMR. spectrum: 1.72 (*s*, 3H, $CH_3-\overset{/}{C}=$), 1.97 (*s*, 3H, $COCH_3$), 4.37 (*s*, 2H, $H_2C=C\langle$), 4.69 (*s*, 2H, $H_2C=C\langle$), 5.70 (broad *s*, $w_{1/2}$ = 7 Hz. $-\underset{\underset{-C=C}{|}}{C}H-OCOCH_3$ · H equatorial; an axial proton would have a broader band). Mass spectrum: 43 (100), 91 (74), 68 (68), 119 (64), 92 (55), 134 (49), 93 (47), 79 (37), 84 and 106 (36), 41, 67, and 105 (34), 39 (22), 77 and 152 (21), 53 and 117 (18), 193 ($M^{+\cdot}$, < 1).

(±)-*4-Acetoxymentha-1.8-diene* (**11**). A solution of 15 g of 4-hydroxymentha-1.8-diene in 30 ml of dry dimethylaniline was stirred at 0° while a mixture of 8 g of acetyl chloride and 5 g of acetic anhydride was added dropwise. The mixture was heated at 40° for 5 hr, then cooled and poured into ice-cold 5% sulphuric acid. The product was extracted into ether, and the ethereal phase washed with 20% aqueous sulphuric acid until all the dimethylaniline had been removed, then with sodium hydrogencarbonate and finally with water. After removal of the ether, the residue (15 g) was distilled, bp. 97°/10 Torr, but it still contained a trace of alcohol as shown by thin layer chromatography (the alcohol and acetate have the same retention times on Carbowax columns). Final purification of a sample for analysis was by chromatography in benzene on a column of silica gel, and redistillation. Mass spectrum: 134 (100), 119 (94), 43 (66), 91 (45), 41 (41), 93 (28), 105 (25), 69 (24), 84 (23), 39, 77, 79 (16–17).

$C_{12}H_{18}O_2$ Calc. C 74.19 H 9.34% Found C 73.92 H 9.33%

Pyrolyses. These were carried out by introducing a 10% solution of the acetate in benzene to the top of a tube, 33 cm in length and 2.5 mm i.d., filled with glass helices, through which a current of dry nitrogen was flowing. The pyrolysate was condensed into a solution of sodium carbonate (10%). In this way, with either acetate **11** or acetates **10**, a benzene solution of a mixture of hydrocarbons was obtained that was purified directly by preparative gas chromatography, without evaporation of the benzene. Preparative gas chromatography on a silicone oil column gave two peaks in the ratio 1:2, the first of which was pure *mentha-1.3.8-triene*. NMR. spectrum: 1.80 and 1.88 (each *s*, 3H, $CH_3-\overset{/}{C}=$), 2.25 (4 lines, 4H, $-CH_2CH_2-$), 4.83, 4.97 (2H, $\rangle C=CH_2$), 5.66 and 5.90 (two *d*, *AB* system, J_{ab} = 6 and 13.5, $-CH=C\langle$). Mass spectrum: 119 (100), 134 (93), 91 (83), 41 (35), 105 (32), 77 (25), 39 and 93 (24), 92 (23), 79 (21), 117 (19), 65

(14), 51 and 115 (12); fragments at 53, 63, 78, 103, 106, and 132 (5–10). Uv. spectrum: λ_{max}^{EtOH} 236.5 nm ε_{max} 11950).

Rechromatography of the second peak on a column of Carbowax again gave two peaks in the ratio 1:1, the second of which proved to be identical with 4-isopropenyltoluene. The first peak was *mentha-1.4.8-triene:* NMR. spectrum: 1.68 and 1.88 (each *s*, 3H, $CH_3-\overset{\diagup}{C}=$), 2.71 (broad *s*, 4H, $-CH_2CH_2-$), 4.83 (broad *s*, 4H, $>C=CH_2$), 5.40 and 5.78 (*m*, $w_{1/2}$ for both signals 5 Hz, 1H each, $-CH=C<$). Mass spectrum: 119 (100), 91 (91), 134 (82), 41 (39), 92, 93, 105 (35), 77 (30), 39 and 79 (24), 117 (22), 65 (15), 51 and 115 (13); fragments at 53, 55, 63, 78, 103, 106, 132, and 133 (5–10). Uv. spectrum: λ_{max}^{EtOH} 303 nm (ε_{max} 14173).

$C_{10}H_{14}$ Calc. C 89.49 H 10.51% Found C 89.21 H 10.21%

Reaction of limonene with mercuric acetate. A mixture of limonene (20 g) and mercuric acetate (46 g) was heated at 140° in a nitrogen atmosphere, then distilled at 10 Torr. A fraction weighing 12 g distilled below 110°/10 Torr, and was redistilled on the spinning band column, when it was separated into unchanged limonene (9 g, bp. 53–54°/10 Torr) and isopropyltoluene (bp. 59–62°/10 Torr). The residue from this distillation (2 g) consisted almost entirely of mentha-1.4.8-triene and polymerized material.

Among the many products present in the residue from the first distillation of this experiment, the following were characterized by chromatography on silica gel, then comparison with authentic samples: mentha-1.4(8)-dien-9-yl acetate (**10a** or **b**) and *trans*-carveyl acetate (**8**).

The assistance of Mr. *Michel Jaccard* for preparative gas chromatography is gratefully acknowledged. We are indebted to Dr. *K.-H. Schulte-Elte* for several samples of authentic materials in addition to the acetate **10** already mentioned. Most useful suggestions and discussion were offered by Dr. *G. Ohloff*.

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